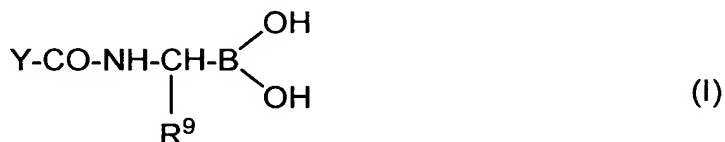




### *Amendments to the Claims*

The listing of claims will replace all prior versions, and listings of claims in the application.

1. (currently amended) A parenteral pharmaceutical formulation comprising a therapeutically effective amount of a pharmaceutically acceptable base addition salt of a boronic acid of formula (I):



wherein

Y comprises a hydrophobic moiety which, together with the aminoboronic acid residue -NHCH(R<sup>9</sup>)-B(OH)<sub>2</sub>, has affinity for the substrate binding site of thrombin; and

R<sup>9</sup> is a straight chain alkyl group interrupted by one or more ether linkages and in which the total number of oxygen and carbon atoms is 3, 4, 5 or 6 or R<sup>9</sup> is -(CH<sub>2</sub>)<sub>m</sub>-W where m is from 2, 3, 4 or 5 and W is -OH or halogen.

2. (original) The formulation of claim 1 wherein R<sup>9</sup> is an alkoxyalkyl group.
3. (original) The formulation of claim 1 wherein YCO- comprises an amino acid residue which binds to the S2 subsite of thrombin, the amino acid residue being N-terminally linked to a moiety which binds the S3 subsite of thrombin.
4. (original) The formulation of claim 1 wherein Y comprises a dipeptide which binds to the S3 and S2 binding sites of thrombin.

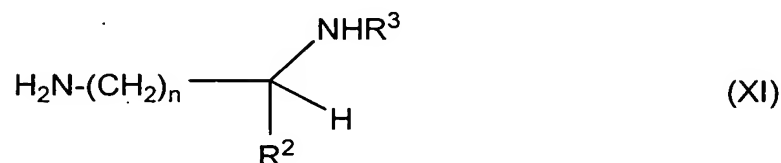
5. (currently amended) The formulation of claim 4 wherein the S3-binding amino acid residue is of (R)-configuration, the S2-binding residue is of (S)-configuration, and the fragment  $\text{-NHCH(R}^9\text{)-B(OH)}_2$  is of (R)-configuration.

6. (previously presented) The formulation of claim 5 wherein  $\text{R}^9$  is an alkoxyalkyl group.

7. (original) The formulation of claim 1 wherein the boronic acid has a  $\text{K}_i$  for thrombin of about 100 nM or less.

8. (original) The formulation of claim 1 wherein the salt comprises a salt of the boronic acid with metal or a strongly basic organic nitrogen-containing compound.

9. (original) The formulation of claim 1 wherein the salt comprises a salt of the boronic acid with an alkali metal, an aminosugar, a guanidine or an amine of formula (XI):



where  $n$  is from 1 to 6,  $\text{R}^2$  is H, carboxylate or derivatised carboxylate,  $\text{R}^3$  is H,  $\text{C}_1\text{-C}_4$  alkyl or a residue of a natural or unnatural amino acid.

10. (original) The formulation of claim 4 wherein the Y dipeptide is N-terminally protected or N-terminally unprotected, and the peptide linkages in the dipeptide are unsubstituted or independently N-substituted by a  $\text{C}_1\text{-C}_{13}$  hydrocarbonyl, wherein the  $\text{C}_1\text{-C}_{13}$  hydrocarbonyl contains no heteratoms or at least one in-chain or in-ring

nitrogen, oxygen or sulfur atom, and the C<sub>1</sub>-C<sub>13</sub> hydrocarbyl is unsubstituted or substituted by a substituent selected from halo, hydroxy and trifluoromethyl.

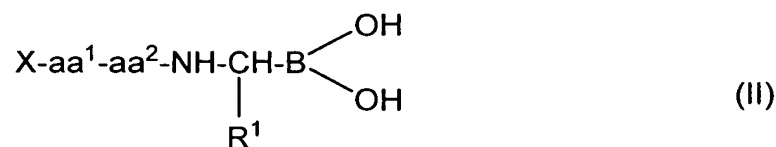
11. (original) The formulation of claim 1 wherein the salt consists essentially of an acid salt in which one B-OH group of formula (I), when trigonally represented, remains protonated.

12. (original) The formulation of claim 9 wherein the salt comprises boronate ions derived from the peptide boronic acid and has a stoichiometry consistent with the boronate ions carrying a single negative charge.

13. (original) The formulation of claim 6 wherein the salt consists essentially of a monosodium or monolithium salt of the boronic acid.

14. (original) The pharmaceutical formulation of claim 9 which is adapted for intravenous administration.

15. (original) A formulation in parenteral dosage form comprising a therapeutically effective amount of a pharmaceutically acceptable base addition salt of a boronic acid of formula (II):



where:

X is H or an amino-protecting group;

aa<sup>1</sup> is an amino acid residue having a hydrocarbyl side chain containing no more than 20 carbon atoms and comprising at least one cyclic group having up to 13 carbon atoms;

aa<sup>2</sup> is an imino acid residue having from 4 to 6 ring members;

R<sup>1</sup> is a group of the formula -(CH<sub>2</sub>)<sub>s</sub>-Z, where s is 2, 3 or 4 and Z is -OH, -OMe, -OEt or halogen.

16. (currently amended) The formulation of claim 15 wherein aa<sup>1</sup> is selected from Phe, Dpa or and wholly or partially hydrogenated analogues thereof.

17. (original) The formulation of claim 16 wherein aa<sup>1</sup> is of R-configuration.

18. (original) The formulation of claim 15 wherein aa<sup>2</sup> is a residue of an imino acid of formula (IV)



where R<sup>11</sup> is -CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-, -S-CH<sub>2</sub>-, -S-C(CH<sub>3</sub>)<sub>2</sub>- or -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, and, when the formula (IV) ring is 5- or 6-membered, the formula (IV) ring is unsubstituted or is substituted at one or more -CH<sub>2</sub>- groups by from 1 to 3 C<sub>1</sub>-C<sub>3</sub> alkyl groups.

19. (original) The formulation of claim 18 wherein aa<sup>2</sup> is of S-configuration.

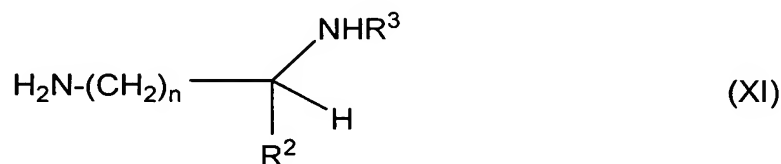
20. (original) The formulation of claim 15, wherein aa<sup>1</sup>-aa<sup>2</sup> is (R)-Phe-(S)-Pro and the fragment -NH-CH(R<sub>1</sub>)-B(OH)<sub>2</sub> is of R-configuration.

21. (original) The formulation of claim 16 wherein the boronic acid is of formula (VIII):



wherein X is  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-C(O)-}$ ,  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-S(O)}_2\text{-}$ ,  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-NH-C(O)-}$  or  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-O-C(O)-}$ , wherein p is 0, 1, 2, 3, 4, 5 or 6 and  $\text{R}^6$  is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a  $\text{C}_5\text{-C}_6$  cyclic group;  $\text{C}_1\text{-C}_4$  alkyl and  $\text{C}_1\text{-C}_4$  alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a  $\text{C}_5\text{-C}_6$  cyclic group.

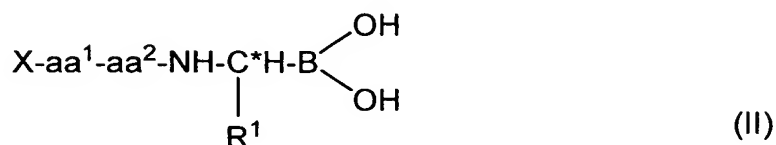
22. (currently amended) The formulation of claim 16 wherein the salt comprises a salt of the boronic acid with an alkali metal, an aminosugar, a guanidine or an amine of formula (XI):



where n is from 1 to 6,  $\text{R}^2$  is H, carboxylate or derivatised carboxylate,  $\text{R}^3$  is H,  $\text{C}_1\text{-C}_4$  alkyl or a residue of a natural or unnatural amino acid.

23. (original) A pharmaceutical product comprising a sealed container containing in the form of a finely divided solid, ready for reconstitution to form a liquid parenteral formulation, a therapeutically effective amount of a boronate salt which

consists essentially of a single pharmaceutically acceptable base addition salt of a boronic acid formula (II):



where:

X is H or an amino-protecting group;

aa<sup>1</sup> is an amino acid residue of R-configuration having a hydrocarbyl side chain containing no more than 20 carbon atoms and comprising at least one cyclic group having up to 13 carbon atoms;

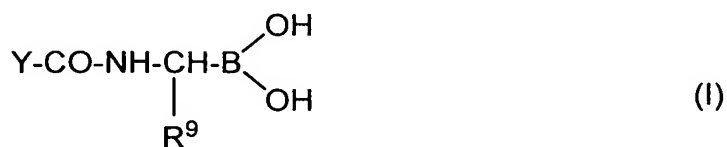
aa<sup>2</sup> is an imino acid residue of S-configuration having from 4 to 6 ring members;

C\* is a chiral centre of R-configuration; and

R<sup>1</sup> is a group of the formula -(CH<sub>2</sub>)<sub>s</sub>-Z, where s is 2, 3 or 4 and Z is -OH, -OMe, -OEt or halogen.

24. (currently amended) A pharmaceutical formulation adapted for parenteral administration, whether directly or after combining with a liquid, and comprising

a) a first species selected from a boronic acid of formula (I), or said boronic acid when in the form of boronate ions of said boronic acid, or equilibrium forms of said boronic acid and said boronate ions, or combinations thereof:



wherein

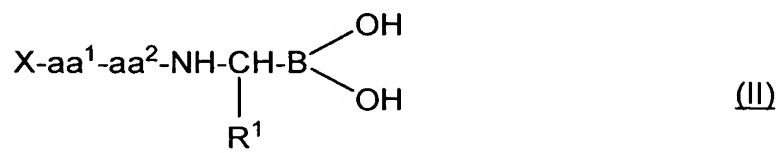
Y comprises a hydrophobic moiety which, together with the aminoboronic acid residue  $\text{-NHCH(R}^9\text{)-B(OH)}_2$ , has affinity for the substrate binding site of thrombin; and  $\text{R}^9$  is a straight chain alkyl group interrupted by one or more ether linkages and in which the total number of oxygen and carbon atoms is 3, 4, 5 or 6 or  $\text{R}^9$  is  $\text{-(CH}_2\text{)}_m\text{-W}$  where m is from 2, 3, 4 or 5 and W is  $\text{-OH}$  or halogen; and

(b) a second, pharmaceutically acceptable, species selected from metal ions and strongly basic organic nitrogen containing compounds ~~having a  $\text{pK}_b$  of about 7 or more~~[[,]].

25. (currently amended) A method of ~~inhibiting thrombin in the prophylaxis or therapy of disease~~ treating or preventing thrombosis, comprising parenterally administering to a mammal suffering from, or at risk of suffering from, thrombosis a therapeutically effective amount of the salt defined in claim 1.

26. (currently amended) A ~~method for~~ The method of claim 25, wherein said treating or preventing thrombosis comprises preventing thrombosis in a haemodialysis circuit of a patient, ~~for~~ preventing a cardiovascular event in a patient with end stage renal disease, ~~for~~ preventing venous thromboembolic events in a patient receiving chemotherapy through an indwelling catheter, ~~for~~ preventing thromboembolic events in a patient undergoing a lower limb arterial reconstructive procedure, or ~~for treating by way of therapy or prophylaxis~~ treating or preventing an arterial disease selected from acute coronary syndromes, cerebrovascular thrombosis, peripheral arterial occlusion and arterial thrombosis resulting from atrial fibrillation, valvular heart disease, arterio-venous shunts, indwelling catheters ~~or~~ and coronary stents, ~~the method comprising parenterally~~

~~administering to a mammal a therapeutically effective amount of the salt defined in claim~~  
~~16~~ and wherein the salt is a pharmaceutically acceptable base addition salt of a boronic  
acid of formula (II):



where:

X is H or an amino-protecting group;

aa<sup>1</sup> is selected from Phe, Dpa and wholly or partially hydrogenated analogues  
thereof;

aa<sup>2</sup> is an imino acid residue having from 4 to 6 ring members; and

R<sup>1</sup> is a group of the formula -(CH<sub>2</sub>)<sub>s</sub>-Z, where s is 2, 3 or 4 and Z is -OH, -OMe,  
-OEt or halogen.

27. (withdrawn) A method for making a salt of claim 1, comprising:

combining in a solvent diethanolamine and an ester of a boronic acid as defined in claim 1;

allowing or causing a precipitate to form and recovering the precipitate;

converting the precipitated material into the free organoboronic acid by contacting the precipitated material with an aqueous acid or base; and

reacting the organoboronic acid with a base of a pharmaceutically acceptable base to form to a salt as defined in claim 1.



28. (original) A medicament adapted for parenteral administration and comprising a therapeutically effective amount of a pharmaceutically acceptable base addition salt of a boronic acid which is a selective thrombin inhibitor and has a neutral aminoboronic acid residue capable of binding to the thrombin S1 subsite linked through a peptide linkage to a hydrophobic moiety capable of binding to the thrombin S2 and S3 subsites, the salt comprising a cation having a valency n and having an observed stoichiometry consistent with a notional stoichiometry (boronic acid:cation) of n:1.

29. (currently amended) A The medicament of claim 28 wherein the boronic acid has a  $K_i$  for thrombin of about 100 nM or less.

30. (previously presented) The method of claim 25 wherein the boronic acid is of formula (VIII):



wherein X is  $\text{R}^6-(\text{CH}_2)_p-\text{C}(\text{O})-$ ,  $\text{R}^6-(\text{CH}_2)_p-\text{S}(\text{O})_2-$ ,  $\text{R}^6-(\text{CH}_2)_p-\text{NH}-\text{C}(\text{O})-$  or  $\text{R}^6-(\text{CH}_2)_p-\text{O}-\text{C}(\text{O})-$ , wherein p is 0, 1, 2, 3, 4, 5 or 6 and  $\text{R}^6$  is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a  $\text{C}_5-\text{C}_6$  cyclic group;  $\text{C}_1-\text{C}_4$  alkyl and  $\text{C}_1-\text{C}_4$  alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a  $\text{C}_5-\text{C}_6$  cyclic group.

31. (previously presented) The method of claim 30, wherein X is  $\text{R}^6-(\text{CH}_2)_p-\text{O}-\text{C}(\text{O})-$ .

32. (previously presented) The method of claim 31, wherein  $R^6$  is a 6-membered cyclic group that is unsubstituted and p is 1.

33. (previously presented) The method of claim 25, wherein the salt is an alkali metal salt.

34. (previously presented) The method of claim 33, wherein the alkali metal salt is a sodium salt.

35. (previously presented) The method of claim 26 wherein the boronic acid is of formula (VIII):



wherein X is  $R^6-(CH_2)_p-C(O)-$ ,  $R^6-(CH_2)_p-S(O)_2-$ ,  $R^6-(CH_2)_p-NH-C(O)-$  or  $R^6-(CH_2)_p-O-C(O)-$ , wherein p is 0, 1, 2, 3, 4, 5 or 6 and  $R^6$  is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a  $C_5-C_6$  cyclic group;  $C_1-C_4$  alkyl and  $C_1-C_4$  alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a  $C_5-C_6$  cyclic group.

36. (currently amended) The method of claim 35, wherein X is  $R^6-(CH_2)_p-O-C(O)-$  and p is 0 or 1.

37. (currently amended) The method of claim 36, wherein  $R^6$  X is benzyloxycarbonyl.

38. (previously presented) The method of claim 26, wherein the salt is an alkali metal salt.

39. (previously presented) The method of claim 38, wherein the alkali metal salt is a sodium salt.

40. (currently amended) The formulation of claim 21, wherein X is  $R^6-(CH_2)_p-O-C(O)-$  and p is 0 or 1.

41. (currently amended) The formulation of claim 40, wherein  $R^6$  X is benzyloxycarbonyl.

42. (previously presented) The formulation of claim 21, wherein the formulation is an aqueous solution comprising the salt.

43. (previously presented) The formulation of claim 42, wherein the aqueous solution further comprises a tonicity agent.

44. (previously presented) The formulation of claim 42, wherein the salt is an alkali metal salt.

45. (previously presented) The formulation of claim 44, wherein the alkali metal salt is a sodium salt.

46. (previously presented) The formulation of claim 1, wherein the formulation comprises an aqueous solution of the salt.

47. (currently amended) A method of ~~inhibiting thrombin in the prophylaxis or therapy of disease~~ treating or preventing thrombosis, comprising parenterally administering to a mammal suffering from, or at risk of suffering from, thrombosis the formulation of claim 1.

48. (previously presented) The method of claim 47 wherein the boronic acid is of formula (VIII):



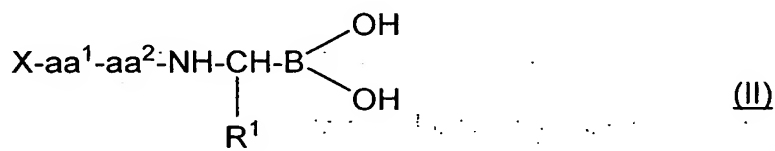
wherein X is  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-C(O)-}$ ,  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-S(O)}_2\text{-}$ ,  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-NH-C(O)-}$  or  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-O-C(O)-}$ , wherein p is 0, 1, 2, 3, 4, 5 or 6 and  $\text{R}^6$  is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a  $\text{C}_5\text{-C}_6$  cyclic group;  $\text{C}_1\text{-C}_4$  alkyl and  $\text{C}_1\text{-C}_4$  alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a  $\text{C}_5\text{-C}_6$  cyclic group.

49. (previously presented) The method of claim 48, wherein the formulation is an aqueous solution comprising the salt.

50. (previously presented) The method of claim 49, wherein the formulation is administered intravenously.

51. (currently amended) ~~A method for~~ The method of claim 25, wherein said treating or preventing thrombosis comprises preventing thrombosis in a haemodialysis circuit of a patient, ~~for~~ preventing a cardiovascular event in a patient with end stage renal disease, ~~for~~ preventing venous thromboembolic events in a patient receiving

chemotherapy through an indwelling catheter, ~~for preventing thromboembolic events in a patient undergoing a lower limb arterial reconstructive procedure, or for treating by way of therapy or prophylaxis~~ treating or preventing an arterial disease selected from acute coronary syndromes, cerebrovascular thrombosis, peripheral arterial occlusion and arterial thrombosis resulting from atrial fibrillation, valvular heart disease, arterio-venous shunts, indwelling catheters ~~or~~ and coronary stents, ~~the method comprising parenterally administering to a mammal a therapeutically effective amount of the salt defined in claim 17~~ and wherein the salt is a pharmaceutically acceptable base addition salt of a boronic acid of formula (II):



where:

X is H or an amino-protecting group;

aa<sup>1</sup> is of R-configuration and is selected from Phe, Dpa and wholly or partially hydrogenated analogues thereof;

aa<sup>2</sup> is an imino acid residue having from 4 to 6 ring members; and

R<sup>1</sup> is a group of the formula -(CH<sub>2</sub>)<sub>s</sub>-Z, where s is 2, 3 or 4 and Z is -OH, -OMe, -OEt or halogen.

52. (previously presented) The method of claim 51 wherein the boronic acid is of formula (VIII):



wherein X is  $R^6-(CH_2)_p-C(O)-$ ,  $R^6-(CH_2)_p-S(O)_2-$ ,  $R^6-(CH_2)_p-NH-C(O)-$  or  $R^6-(CH_2)_p-O-C(O)-$ , wherein p is 0, 1, 2, 3, 4, 5 or 6 and  $R^6$  is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a  $C_5-C_6$  cyclic group;  $C_1-C_4$  alkyl and  $C_1-C_4$  alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a  $C_5-C_6$  cyclic group.

53. (previously presented) The method of claim 52, wherein the formulation is an aqueous solution comprising the salt.

54. (previously presented) The method of claim 53, wherein the formulation is administered intravenously.

55. (previously presented) The method of claim 25, further comprising co-administering at least one further cardiovascular treatment agent.

56. (previously presented) The method of claim 26, further comprising co-administering at least one further cardiovascular treatment agent.

57. (currently amended) A method of ~~inhibiting thrombin in the prophylaxis or therapy of disease~~ treating or preventing thrombosis, comprising parenterally administering to a mammal suffering from, or at risk of suffering from, thrombosis a therapeutically effective amount of the pharmaceutical formulation of claim 24.

58. (previously presented) The formulation of claim 1 which comprises anhydride species of the acid.

59. (previously presented) The formulation of claim 15 which comprises the boronic acid in the form of an anhydride.

60. (previously presented) The formulation of claim 1 wherein the salt is a metal salt of the boronic acid.

61. (previously presented) The formulation of claim 58 wherein the salt is a metal salt of the boronic acid.

62. (previously presented) The formulation of claim 59 wherein the salt is a metal salt of the boronic acid.

63. (previously presented) The formulation of claim 23 wherein the boronic acid is of the formula Cbz-(R)-Phe-(S)-Pro-(R)-boroMpg-OH, boroMpg-OH being a residue of an aminoboronic acid of the formula  $\text{H}_2\text{N}-\text{CH}((\text{CH}_2)_3\text{OMe})\text{B}(\text{OH})_2$ , and wherein the formulation comprises anhydride species of the acid.

64. (previously presented) The formulation of claim 63 wherein the salt is an alkali or alkaline earth metal salt of the boronic acid.

65. (previously presented) The formulation of claim 63, wherein the salt is a monosodium salt of the boronic acid.

66. (withdrawn) The formulation of claim 63, wherein the salt is a hemicalcium salt of the boronic acid.

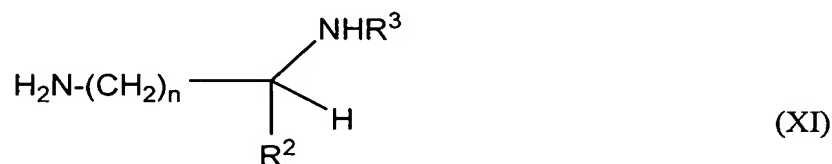
67. (previously presented) The formulation of claim 4 wherein R<sup>9</sup> is 3-methoxypropyl and the carbon atom to which R<sup>9</sup> is bonded comprises a chiral centre of (R)-configuration.

68. (previously presented) The formulation of claim 67 wherein the salt consists essentially of an alkali metal or alkaline earth metal salt.

69. (previously presented) The formulation of claim 67 wherein the salt consists essentially of a sodium salt.

70. (previously presented) The formulation of claim 67 wherein the salt consists essentially of a monosodium salt.

71. (withdrawn) The formulation of claim 67 wherein the salt consists essentially of a salt of the boronic acid with an aminosugar, a guanidine or an amine of formula (XI):



where n is from 1 to 6, R<sup>2</sup> is H, carboxylate or derivatised carboxylate, R<sup>3</sup> is H, C<sub>1</sub>-C<sub>4</sub> alkyl or a residue of a natural or unnatural amino acid.

72. (previously presented) The formulation of claim 67 which comprises an aqueous solution containing the salt.



73. (previously presented) The formulation of claim 67 which comprises the boronic acid in the form of an anhydride.

74. (previously presented) The formulation of claim 67 which is adapted for intravenous formulation and is either in the form of an aqueous solution or is in solid form for making up into an aqueous solution for administration.

75. (previously presented) The formulation of claim 74 wherein the boronic acid is of the formula Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

76. (previously presented) The formulation of claim 75 wherein the salt is an alkali metal salt.

77. (previously presented) The formulation of claim 75 wherein the salt is a sodium salt.

78. (previously presented) The formulation of claim 75 wherein the salt is a monosodium salt.

79. (withdrawn) The formulation of claim 75 wherein the salt is a hemicalcium salt.

80. (withdrawn) The formulation of claim 75 wherein the salt is a hemimagnesium salt.

81. (previously presented) The formulation of claim 1 wherein the boronic acid is of the formula Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

82. (previously presented) The formulation of claim 1 wherein the salt is a metal salt of a boronic acid of the formula Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

83. (previously presented) The formulation of claim 1 wherein the salt is an alkali metal or alkaline earth metal salt of a boronic acid of the formula Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

84. (previously presented) The formulation of claim 1 wherein the salt consists essentially of a monosodium salt of a boronic acid of the formula Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

85. (previously presented) The formulation of claim 84 which comprises anhydride species of the acid.

86. (previously presented) The formulation of claim 84 which does not comprise anhydride species of the acid.

87. (previously presented) The formulation of claim 24 wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge.

88. (currently amended) The formulation of claim 24 wherein the second species is selected from pharmaceutically acceptable metal ions, said metal ions having a valency of n[.,,]; lysine[.,,]; arginine; and ~~or~~ aminosugars[.,,]; wherein the formulation has an observed stoichiometry of first to second species essentially consistent with a notional stoichiometry of 1:1 when the second species is a metal ion with a valency of 1

or is lysine, arginine or an aminosugar, or an observed stoichiometry of n:1 when the second species is a metal ion with a valency of greater than 1.

89. (previously presented) The formulation of claim 24 wherein the boronic acid is of formula (VIII):



wherein X is  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-C(O)-}$ ,  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-S(O)}_2\text{-}$ ,  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-NH-C(O)-}$  or  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-O-C(O)-}$ , wherein p is 0, 1, 2, 3, 4, 5 or 6 and  $\text{R}^6$  is H or a 5 to 13-membered cyclic group which is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen; amino; nitro; hydroxy; a  $\text{C}_5\text{-C}_6$  cyclic group;  $\text{C}_1\text{-C}_4$  alkyl and  $\text{C}_1\text{-C}_4$  alkyl containing, or linked to the cyclic group through, an in-chain O atom, the aforesaid alkyl groups optionally being substituted by a substituent selected from halogen, amino, nitro, hydroxy and a  $\text{C}_5\text{-C}_6$  cyclic group; and boroMpg-OH is a residue of an aminoboronic acid of the formula  $\text{H}_2\text{N-CH}((\text{CH}_2)_3\text{OMe})\text{B(OH)}_2$ .

90. (currently amended) The formulation of claim ~~88~~ 89, wherein X is  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-O-C(O)-}$ .

91. (currently amended) The formulation of claim 89, wherein X is  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-O-C(O)-}$  and  $\text{R}^6$  is a 6-membered cyclic group that is unsubstituted and p is 1.

92. (previously presented) The formulation of claim 91 wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge.

93. (previously presented) The formulation of claim 24 wherein the boronic acid is of formula Cbz-(R)-Phe-(S)-Pro-(R)-boroMpg-OH and the second species comprises sodium ions, boroMpg-OH being a residue of an aminoboronic acid of the formula  $\text{H}_2\text{N}-\text{CH}((\text{CH}_2)_3\text{OMe})\text{B}(\text{OH})_2$ .

94. (previously presented) The formulation of claim 93 which is a solution.

95. (previously presented) The formulation of claim 24 wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge, the boronic acid is of formula Cbz-(R)-Phe-(S)-Pro-(R)-boroMpg-OH, and the second species consists essentially of sodium ions, boroMpg-OH being a residue of an aminoboronic acid of the formula  $\text{H}_2\text{N}-\text{CH}((\text{CH}_2)_3\text{OMe})\text{B}(\text{OH})_2$ .

96. (withdrawn) The formulation of claim 24 wherein the boronic acid is of formula Cbz-(R)-Phe-(S)-Pro-(R)-boroMpg-OH and the second species comprises calcium ions.

97. (withdrawn) The formulation of claim 24 wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge, the boronic acid is of formula Cbz-(R)-Phe-(S)-Pro-(R)-boroMpg-OH, and the second species consists essentially of calcium ions, boroMpg-OH being a residue of an aminoboronic acid of the formula  $\text{H}_2\text{N}-\text{CH}((\text{CH}_2)_3\text{OMe})\text{B}(\text{OH})_2$ .

98. (currently amended) The formulation of claim 24, wherein:

the formulation is a solution,

Y comprises a dipeptide which binds to the S3 and S2 binding sites of thrombin, the S3-binding amino acid residue being of (R)-configuration and the S2-binding residue of (S)-configuration,

the fragment  $\text{-NHCH(R}^9\text{)-B(OH)}_2$  is of (R)-configuration, and

$\text{R}^9$  is methoxypropyl.

99. (previously presented) The formulation of claim 98 wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge.

100. (currently amended) The formulation of claim 24 which is a solution, and wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge, the boronic acid is of formula (VIII):

$\text{X-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)}_2$  (VIII),

wherein X is  $\text{R}^6\text{-(CH}_2\text{)}_p\text{-O-C(O)-}$  and  $\text{R}^6$  is a 6-membered cyclic group that is unsubstituted and p is 1,

and the second species is selected from magnesium, calcium and sodium ions.

101. (currently amended) The formulation of claim 24, wherein:

the formulation is a solid dosage form,

Y comprises a dipeptide which binds to the S3 and S2 binding sites of thrombin, the S3-binding amino acid residue being of (R)-configuration and the S2-binding residue of (S)-configuration,

the fragment -NHCH(R<sup>9</sup>)-B(OH)<sub>2</sub> is of (R)-configuration, and  
R<sup>9</sup> is methoxypropyl.

102. (previously presented) The formulation of claim 101 wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge.

103. (currently amended) The formulation of claim 24 which is a solid dosage form, and wherein the formulation has an observed stoichiometry which would be consistent with the first species being boronate ions carrying a single negative charge, the boronic acid is of formula (VIII):

X-(R)-Phe-(S)-Pro-(R)-boroMpg-OH (VIII);

wherein X is R<sup>6</sup>-(CH<sub>2</sub>)<sub>p</sub>-O-C(O)- and R<sup>6</sup> is a 6-membered cyclic group that is unsubstituted and p is 1,

and the second species is selected from magnesium, calcium and sodium ions.

104. (withdrawn) The formulation of claim 91 wherein the ~~salt~~ second species is an L-arginine salt or an L-lysine salt.

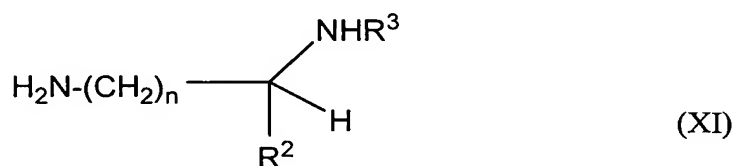
105. (currently amended) The formulation of claim 91 wherein the second species salt is a sodium ions salt.

106. (withdrawn) The formulation of claim 91 wherein the second species salt is a lithium ions salt.

107. (withdrawn) The formulation of claim 91 wherein the second species salt is a glucamine salt.

108. (withdrawn) The formulation of claim 91 wherein the second species salt is a calcium ions or magnesium ions salt.

109. (withdrawn) The formulation of claim 91 which is adapted for intravenous administration, whether directly or after combining with a liquid, wherein the second species salt is ~~a salt of the boronic acid with~~ an aminosugar, a guanidine or an amine of formula (XI):



where n is from 1 to 6, R<sup>2</sup> is H, carboxylate or derivatised carboxylate, R<sup>3</sup> is H, C<sub>1</sub>-C<sub>4</sub> alkyl or a residue of a natural or unnatural amino acid.

110. (previously presented) The formulation of claim 67 further comprising at least one further pharmaceutically active agent.

111. (currently amended) The formulation of claim 110 wherein the further pharmaceutically active agent comprises a cardiovascular treatment agent selected from the group consisting of a lipid-lowering drug[[s]], a fibrate[[s]], niacin, a statin[[s]], a CETP inhibitor[[s]], a bile acid sequestrant[[s]], an anti-oxidant[[s]], a GP IIb/IIIa antagonist[[s]], an aldosterone inhibitor[[s]], an A2 antagonist[[s]], an A3 agonist[[s]], a beta-blocker[[s]], acetylsalicylic acid, a loop diuretic[[s]], an ACE inhibitor[[s]], an antithrombotic agent[[s]] with a different mechanism of action from the salt of formula (I), an antiplatelet agent[[s]], a thromboxane receptor and/or synthetase

inhibitor[[s]], a fibrinogen receptor antagonist[[s]], a prostacyclin mimetic[[s]], a phosphodiesterase inhibitor[[s]], an ADP-receptor (P<sub>2</sub>T) antagonist[[s]], a thrombolytic[[s]], a cardioprotectant[[s]] and a COX-2 inhibitor[[s]], and combinations thereof.

112. (previously presented) The method of claim 25 wherein the ~~formulation comprises an aqueous solution of salt~~ is a sodium salt of a boronic acid of the formula Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>, and wherein the salt is in an aqueous solution.

113. (previously presented) The method of claim 25 wherein the sodium salt is the monosodium salt.

114. (currently amended) The formulation of claim 24 which comprises a mixture of said second species, and wherein:

Y comprises a dipeptide which binds to the S3 and S2 binding sites of thrombin, the S3-binding amino acid residue being of (R)-configuration and the S2-binding residue of (S)-configuration,

the fragment -NHCH(R<sup>9</sup>)-B(OH)<sub>2</sub> is of (R)-configuration, and

R<sup>9</sup> is methoxypropyl.

115. (currently amended) The formulation of claim 1 wherein the organoboronic acid is of the formula Cbz-(R)-Phe-(S)-Pro-(R)-boroMpg-OH, wherein boroMpg-OH is a residue of an aminoboronic acid of the formula H<sub>2</sub>N-CH((CH<sub>2</sub>)<sub>3</sub>OMe)B(OH)<sub>2</sub>, the formulation comprising



a) a first species selected from said boronic acid, said boronic acid when in the form of boronate ions of said boronic acid, ~~or~~ equilibrium forms of said boronic acid and said boronate ions, ~~or~~ and combinations thereof; and

(b) one or a mixture of pharmaceutically acceptable cations.

116. (currently amended) A method for ~~inhibiting thrombin in the treatment or prevention of disease~~ treating or preventing thrombosis in a subject, comprising parenterally administering to the subject a pharmaceutical formulation adapted to result, after administration of the formulation, in the release of boronate species obtainable from a boronic acid as defined in claim 1 and pharmaceutically acceptable cations.

117. (new) A pharmaceutical formulation suitable for intravenous administration, comprising an aqueous solution of a pharmaceutically acceptable base addition salt of Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

118. (new) The formulation of claim 117 wherein the salt is a sodium salt, a lithium salt, an L-arginine salt, an L-lysine salt or an N-methyl-D-glucamine salt.

119. (new) A pharmaceutical formulation suitable for intravenous administration, comprising, in solid form for making up into an aqueous solution for administration, a pharmaceutically acceptable base addition salt of Cbz-(R)-Phe-(S)-Pro-(R)-Mpg-B(OH)<sub>2</sub>.

120. (new) The formulation of claim 119 wherein the salt is a sodium salt, a lithium salt, an L-arginine salt, an L-lysine salt or an N-methyl-D-glucamine salt.